REMARKS/ARGUMENTS

Claims 1, 13-23, 51-55, 68-71 and 74-79 are now active in this application, claims 2-12, 24-50, 56-67 and 72-73 having been cancelled by the present amendment. Claim 1 has been amended to include the limitations of claims 6 and 11. Various claims have been amended to remove improper dependencies and multiple dependencies. New claims 74-79 correspond to original claims 51-55 once multiple dependencies have been separated into single dependencies. All amendments are supported by the claims as originally filed. No new matter has been added by these amendments.

Applicants are also providing herewith a Petition to Make Special on the grounds that the presently claimed invention is used in the treatment of cancer and thus meets the requirements under MPEP 708.02, part X. As noted in the specification at page 3, lines 6-10, the crystal of a salt according to the present invention is useful for the therapy of tumors, and Kaposi's sarcoma. Both of these are forms of cancer, with the latter, Kaposi's sarcoma, being a common form of cancer encountered by those afflicted with HIV/AIDS. In particular, as noted at page 33, beginning at line 20, N-{2-Chloro-4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl}-N'-(5-methyl-3-isoxazolyl)urea has tumor enhancement inhibitory activity in vivo (Pharmacological Test Examples 2, 3, and 4 in WO02/88110). Further, this compound inhibits in vitro the autophosphorylation activity in human KDR intracellular regions caused by stimulation of NIH3T3 cells, which can stably express human KDR, with VEGF (vascular endothelial growth factor) (Pharmacological Test Example 1 in WO 02/88110). Binding of VEGF to KDR, which is present as a receptor of VEGF on cell membranes, causes activation of MAPK (mitogen-activated protein kinase) and the like through autophosphorylation of KDR intracellular regions by tyrosine kinase (Shibuya M, Ito N, Claesson-Welsh L., in Curr. Topics Microbiol Immunol., 237, 59-83 (1999); Abedi, H. and Zachary, I., J. Biol. Chem., 272, 15442-15451 (1997)). The activation of MAPK is

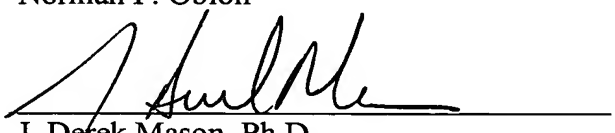
known to play an important role in the growth of vascular endothelial cells in angiogenesis (Merenmies, J. et al., Cell Growth & Differ., 83-10 (1997); and Ferrara, N. and Davis-Smyth, T., Endocr. Rev., 18, 4-25 (1997)). Therefore, the above compound has angiogenesis inhibitory activity. It is known that angiogenesis at pathologic sites is deeply involved mainly in several different diseases, such as tumors, and Kaposi's sacrcoma, (as well as diabetic retinopathy, chronic rheumatism, psoriasis, and atherosclerosis), and in the metastasis of solid tumors (Folkman, J. Nature Med. 1: 27-31 (1995); Bicknell, R., Harris, A. L. Curr. Opin. Oncol. 8: 60-65 (1996)). Accordingly, the present invention falls within the definition provided for in MPEP 708.02, part X for treating the present application as Special for expedited examination.

In order to expedite that examination, Applicants have significantly limited the claims to the most preferred embodiment of the invention.

Applicants submit that the application is ready for expedited examination, and early notification of such action is earnestly solicited.

Respectfully submitted,

OBLON, SPIVAK, McCLELLAND,
MAIER & NEUSTADT, P.C.
Norman F. Oblon



J. Derek Mason, Ph.D.
Attorney of Record
Registration No. 35,270

Customer Number
22850

Tel: (703) 413-3000
Fax: (703) 413 -2220
(OSMMN 06/04)